Radiology

REVIEWS AND COMMENTARY • REVIEW

# Interpretation, Reporting, and Clinical Applications of Liver MR Elastography

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Conflicts of interest are listed at the end of this article.

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Chronic liver disease is highly prevalent and often leads to fibrosis or cirrhosis and complications such as liver failure and hepatocellular carcinoma. The diagnosis and staging of liver fibrosis is crucial to determine management and mitigate complications. Liver biopsy for histologic assessment has limitations such as sampling bias and high interreader variability that reduce precision, which is particularly challenging in longitudinal monitoring. MR elastography (MRE) is considered the most accurate noninvasive technique for diagnosing and staging liver fibrosis. In MRE, low-frequency vibrations are applied to the abdomen, and the propagation of shear waves through the liver is analyzed to measure liver stiffness, a biomarker for the detection and staging of liver fibrosis. As MRE has become more widely used in clinical care and research, different contexts of use have emerged. This review focuses on the latest developments in the use of MRE for the assessment of liver fibrosis; provides guidance for image acquisition and interpretation; summarizes diagnostic performance, along with thresholds for diagnosis and staging of liver fibrosis; discusses current and emerging clinical applications; and describes the latest technical developments.

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*Supplemental material is available for this article.*

In patients with chronic liver disease, the diagnosis and staging of liver fibrosis is crucial to inform management, with treatment more effective when initiated at early stages (1). While historically biopsy has been the reference standard for the diagnosis and staging of liver fibrosis, it is limited by risk of complications, high cost, sampling error, and high intra- and interobserver variability (1–3). Additionally, different histologic staging systems have been proposed, which can introduce staging discrepancies (4). To address these issues, minimally invasive or noninvasive techniques have been investigated.

As fibrosis develops, quantification of changes in liver stiffness can provide an important assessment of disease severity (5,6). Elastographic techniques indirectly measure tissue stiffness by assessing the mechanical properties of the tissue. Different elastographic techniques assess different stiffness-related parameters (eg, shear stiffness or Young, or elastic, modulus), although the underlying principle is the measurement of shear-wave propagation. In normal liver, the tissue is softer, resulting in shear waves with higher attenuation and slower propagation. As fibrosis develops, liver stiffness increases and wave propagation becomes faster, with longer wavelengths and lower attenuation (7). MR elastography (MRE) stiffness measurements provide the highest classification accuracy for noninvasive staging of liver fibrosis (8).

In this article, we explain general concepts of MRE, provide guidance on analysis and reporting, summarize the diagnostic performance of MRE and thresholds for diagnosis and staging of liver fibrosis, and discuss current and emerging clinical applications and the latest technical developments.

## Introduction to MRE

### General Concepts

MRE uses an external driver to produce and transmit mechanical low-frequency vibrations onto the abdominal wall over the liver. Phase-contrast sequences with motion-encoding gradients are used to image shear-wave propagations, and an inversion algorithm converts the wave propagation information into quantitative stiffness maps (ie, elastograms). The standard imaging marker measured is "shear stiffness," expressed in kilopascals (7). Acquisition is performed using the end-expiration breath-hold technique. Clinical sequences and postprocessing steps are described in Appendix S1.

### Interpretation and Reporting

To avoid sample bias, regions of interest covering as much liver parenchyma as possible are recommended (9). Regions of interest should be placed on the stiffness maps within areas that display parallel wave motion

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## Abbreviations

AST = aspartate aminotransferase, FIB-4 = Fibrosis-4, MAFLD = metabolic dysfunction–associated fatty liver disease, MASH = metabolic dysfunction–associated steatohepatitis, MAST = MRI-AST, MRE = MR elastography


## Summary

This review focuses on the clinical implementation of MR elastography for assessing liver fibrosis, simple thresholds for staging, current and emerging clinical applications, and latest technical developments.


## Essentials

- The Quantitative Imaging Biomarkers Alliance provides guidance to standardize imaging acquisition and interpretation for MR elastography (MRE).
- The Liver Imaging Reporting and Data System Quantitative Imaging Working Group and the Society of Abdominal Radiology Liver Fibrosis Disease Focus Panel recommend a common set of simple thresholds applicable to most liver etiologies for the diagnosis and staging of liver fibrosis: 3.0 kPa for F1 or higher, 3.5 kPa for F2 or higher, 4.0 kPa for F3 or higher, and 5.0 kPa for F4.
- Among noninvasive techniques, MRE provides the highest accuracy for detecting and staging liver fibrosis.

(on the wave images) and have valid pixel values (as indicated by the confidence map), while avoiding artifacts, large vessels, lesions, and the outer 1 cm below the capsule (Fig 1). Once the optimal regions of interest are drawn in areas of reliable data on each image section, the mean per-section stiffness is recorded, and the mean for four sections is calculated (10). Mean liver stiffness is reported as a continuous variable (in kilopascals), commonly with stiffness thresholds that relate to the stage of fibrosis (Fig 2).

Variations in published thresholds likely stem from differences in study populations, inclusion of different etiologies, variability in interpretation of biopsy as reference standard, and other confounders (Fig 3). To address this issue and simplify the interpretation of MRE stiffness in clinical care, the Liver Imaging Reporting and Data System Quantitative Imaging Working Group and the Society of Abdominal Radiology Liver Fibrosis Disease Focus Panel recommend a common set of simple thresholds applicable to most etiologies: 3.0 kPa for stage F1 or higher, 3.5 kPa for stage F2 or higher, 4.0 kPa for stage F3 or higher, and 5.0 kPa for stage F4 (9,11). These thresholds were derived from consensus interpretation of multiple studies and meta-analysis and were endorsed by 88% (22 of 25) of the members in the working group.

In longitudinal studies, the relative change (expressed as a percentage) in the elastographic stiffness value should be reported since a change exceeding 20% between examinations can be interpreted as a true biologic change (10,12), whereas smaller changes may be attributable to measurement variability. Caution is required when interpreting change in patients with viral hepatitis undergoing antiviral therapy, because a rapid drop in stiffness values may reflect a reduction in inflammation rather than fibrosis reversal (13). Fluctuations in liver stiffness due to inflammation may also be observed in other types of hepatitis during treatment (eg, autoimmune hepatitis) (14), though further research is needed to fully understand this process. Other potential pitfalls and confounders in interpretation are summarized in Table 1.

### Diagnostic Performance

Early literature focused on the overall feasibility and accuracy of MRE to diagnose liver fibrosis, and since 2006, more than 500 articles have been published, with several focusing on the diagnostic performance of different stiffness thresholds for staging liver fibrosis. The diagnostic performance of MRE for advanced (≥F3) fibrosis is excellent, with most studies reporting greater than 80% sensitivity and greater than 90% specificity. More granular discriminations (ie, F1 vs F2 vs F3 vs F4) also show high performance (15–18). Table 2 summarizes the diagnostic performance of MRE for staging liver fibrosis reported in the literature. In a large meta-analysis by Singh et al (8) including 12 studies and 697 individual patients with different chronic liver diseases from Europe and the United States, the area under the receiver operating characteristic curve values for discriminating any (≥F1), significant (≥F2), or advanced fibrosis (≥F3) or cirrhosis (≥F4) were 0.84, 0.88, 0.93, and 0.92,

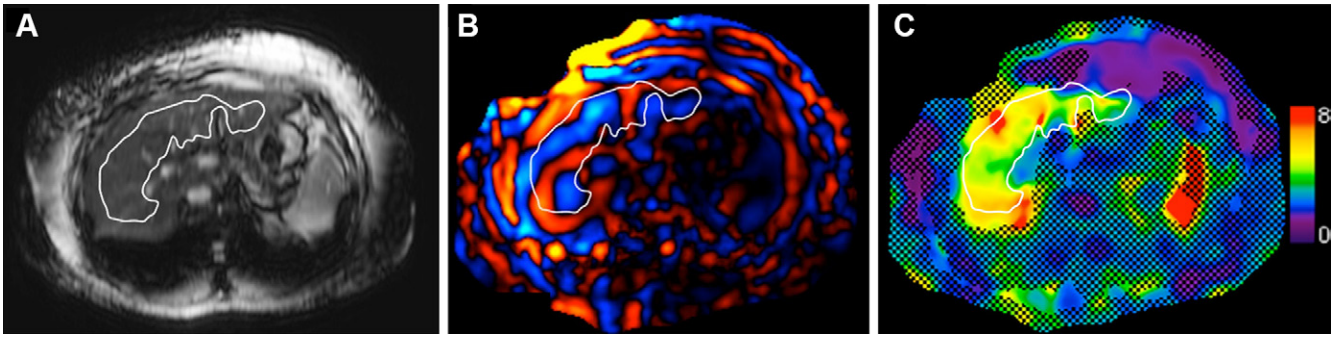


**Figure 1:** RSNA Quantitative Imaging Biomarkers Alliance recommendations for region of interest placement and measurement of shear-wave propagation in MR elastography. A region of interest (outline) is drawn on the **(A)** axial source magnitude image, with simultaneous visualization of the **(B)** wave image and the **(C)** elastogram with overlaid confidence map (hatching), in such a way as to include the largest portion of liver tissue. The region of interest should be placed on individual image sections excluding areas of low wave propagation, large vessels, focal lesions, marginal liver tissues (to avoid edge effect), and areas identified by the inversion algorithm as invalid (hatching in **C**). The mean liver stiffness is reported by recording the mean stiffness value of each region of interest (ie, each section) and then calculating the mean value for all sections, weighted by the size of the region of interest. In the wave image **(B)**, red indicates peaks and blue indicates troughs. Highly saturated colors indicate high wave amplitude, and black indicates low wave amplitude. Color bar in the elastogram **(C)** indicates stiffness range.

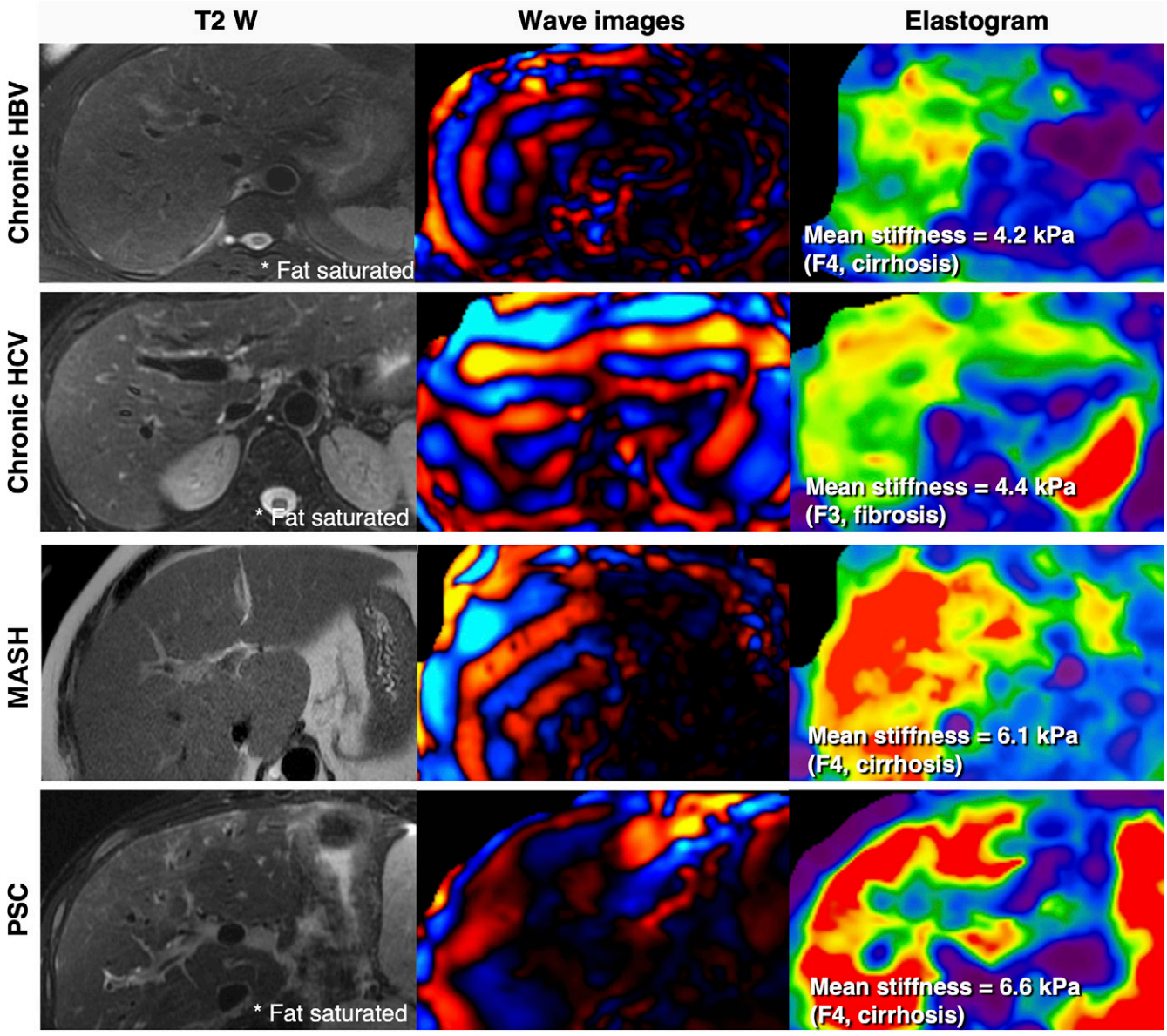


**Figure 2:** Example axial T2-weighted (T2 W) MRI scans (left), wave images (middle), and elastograms (right) illustrating the contexts of use of MR elastography in patients with advanced fibrosis with different liver disease etiologies. The reported stiffness threshold for fibrosis stages may vary based on differences in study population and reference standard (ie, histologic examination) sampling variability. Based on consensus interpretation of multiple studies and meta-analysis, and to simplify the interpretation of MR elastographic stiffness in clinical care, a common set of simple thresholds is recommended regardless of the underlying etiology of chronic liver disease: 3.0 kPa for stage F1 or higher, 3.5 kPa for stage F2 or higher, 4.0 kPa for stage F3 or higher, and 5.0 kPa for stage F4. HBV = hepatitis B virus infection, HCV = hepatitis C virus infection, MASH = metabolic dysfunction–associated steatohepatitis, PSC = primary sclerosing cholangitis.

respectively. High reproducibility—with low bias (–0.03 to 0.11 kPa) and narrow limits of agreement—has been reported, with accurate fibrosis classification using different MRI scanners and at different imaging centers (19,20).

## Current and Emerging Clinical Applications of MRE

### Liver Fibrosis Diagnosis, Staging, and Monitoring

Several histologic staging systems for liver fibrosis have been proposed, most of which are etiology specific. For simplicity and improved communication in clinical practice, two terms are widely accepted for evaluating the utility of noninvasive markers of liver fibrosis: Significant fibrosis refers to stage F2 or higher (F3 for Ishak score), and advanced fibrosis refers to stage F3 or higher (F4 for Ishak score). However, translating stiffness values to categorical fibrosis stages may ignore the biologic complexity and continuous spectrum of liver disease. This is particularly important once cirrhosis is established, as patients with cirrhosis are grouped in a single category in most histologic systems, without further categorization that may relate to severity or outcome prediction. Thus, interpreting liver stiffness as a continuous variable to inform clinical management may provide a better prognostic correlation (Fig 4) (21).

Imaging-based elastographic techniques to measure liver stiffness have been implemented using US and MRI technology.

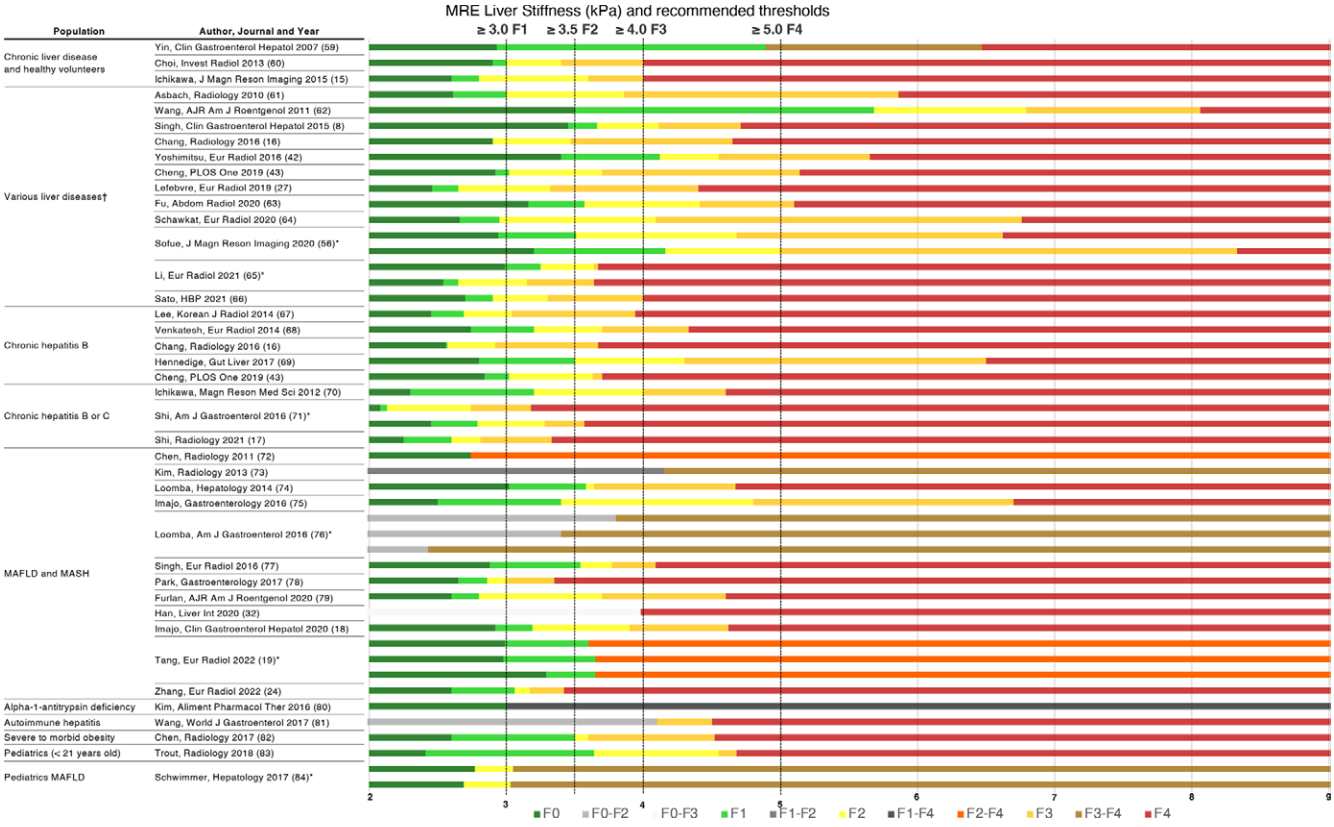


**Figure 3:** Graph shows reported MR elastographic (MRE) stiffness thresholds (in kilopascals) for fibrosis staging. Dotted lines represent the thresholds recommended by the Liver Imaging Reporting and Data System Quantitative Imaging Working Group: 3.0 kPa or higher for stage F1 (mild fibrosis), 3.5 kPa or higher for stage F2 (significant fibrosis), 4.0 kPa or higher for stage F3 (advanced fibrosis), and 5.0 kPa or higher for stage F4 (cirrhosis). * = These studies report results for different sequences, frequencies, readers, or stiffness thresholds investigated. † = "Various liver diseases" includes hepatitis B virus infection, hepatitis C virus infection, metabolic dysfunction–associated steatohepatitis (MASH), and autoimmune hepatitis. MAFLD = metabolic dysfunction–associated fatty liver disease.

US-based elastographic methods, discussed in detail elsewhere (7,22), have the advantage of higher accessibility, with satisfactory accuracy in the clinical setting. Limitations include reduced accuracy in patients with large body habitus or narrow intercostal spaces, and limited intra- and interreader agreement (23). MRE provides a larger field of view than US-based elastographic methods, reducing sampling variability, with overall higher accuracy for staging liver fibrosis, particularly at early stages (24). Further, the high interdevice and interoperator reproducibility of MRE is advantageous for longitudinal monitoring and assessment of treatment response in clinical care and clinical trials (25).

## Improved Participant Selection for Clinical Trials

Noninvasive identification of patients with early-stage fibrosis who could potentially benefit from pharmacologic therapy is currently a major unmet clinical gap (26). For inclusion in clinical trials of therapies for metabolic dysfunction–associated fatty liver disease (MAFLD), the U.S. Food and Drug Administration and European guidelines require a diagnosis of significant (≥F2) liver fibrosis stage, but selecting potential candidates without liver biopsy can be challenging. Among noninvasive tests, MRE provides the highest accuracy for detecting and staging liver fibrosis (ie, F1 vs F2) (24,27). Therefore, MRE-determined liver stiffness may provide a biomarker for treatment selection and enrollment in phase II clinical trials, and disease-specific cutoffs can be considered. For phase III trials, regulatory agencies currently continue to require histologic confirmation of fibrosis staging. In this setting, MRE may be used for cohort enrichment by excluding patients who otherwise would undergo biopsy without the required stage of fibrosis.

## Ruling in or Ruling out Liver Fibrosis

The American Association for the Study of Liver Diseases recommends noninvasive tests to help identify advanced fibrosis risk, optimizing the benefit-to-risk ratio for invasive procedures like biopsy. MRE, with its high specificity and positive predictive value, is an ideal method to help identify high-risk patients who should undergo liver biopsy. Conversely, the high sensitivity and negative predictive value of MRE mean that it can help rule out disease, which is crucial for determining which patients can be treated by primary care physicians and which patients need hepatologist referral. Unlike many other noninvasive tests, MRE excels in both ruling out and ruling in liver fibrosis, making it an ideal choice for clinical practice (28).

## Risk Stratification of Liver-related Complications

Several studies highlight the potential utility of MRE in predicting disease progression and liver-related complications. In patients with hepatitis C virus infection, liver stiffness is an independent risk factor for cirrhosis development, with negligible

**Table 1: Confounders and Technical Pitfalls Affecting MRE Interpretation**

| Confounder or Pitfall | Description | Mitigation Strategies |
|---|---|---|
| Biologic confounders | | |
| Inflammation | Liver inflammation causes edema and congestion contained by the liver capsule, which raises the stiffness and viscosity measured using elastographic techniques; this can lead to overestimation of stiffness measurements and misclassification of early fibrosis | If there are findings to suggest concomitant liver inflammation, cautious interpretation of stiffness values should consider the clinical picture, particularly during longitudinal assessment |
| Cholestasis and venous congestion | Both increased biliary pressure in obstructive cholestasis and increased venous congestion due to increased outflow pressure (eg, Fontan procedure) can increase liver stiffness and therefore lead to overestimation of fibrosis stage | In patients with obstructive cholestasis, MRE could be postponed until the obstruction has been addressed or the biliary tree decompressed; caution in interpretation of stiffness values is recommended in the setting of known venous congestion |
| Postprandial state | Postprandial state is associated with mild increases in liver stiffness; the overall effect of postprandial state is small in normal liver but quite significant in fibrotic liver and can change fibrosis staging | MRE should be performed in the fasting state (>4 h) |
| Technical pitfalls | | |
| Improper hardware setup | Inadequate propagation of mechanical waves in the liver can occur due to improper driver placement, a disconnected passive driver, or improper attachment to the body; tissue stiffness is frequency dependent, so using a nonstandard vibration frequency (ie, different than 60 Hz) will result in incorrect measurements | Quality assessment is recommended before terminating the examination; if there are signs of driver disconnection or misplacement (eg, absent vibration artifacts underneath the driver or atypical artifacts seen on magnitude images), imaging should be repeated after reconnection and replacement of the driver; use of nonstandard vibration frequencies should be avoided |
| Right vs left liver lobes | Cardiac pulsation onto the left liver lobe may interfere with the imaging of propagating shear waves and result in unreliable stiffness measurements | The driver should be placed in the right anterior axillary line over the liver or, alternatively, in the right axillary line in patients with difficult anatomy (eg, large breast, catheter ports); the left lobe should be avoided, when possible, during drawing and selection of the region of interest |
| Liver iron overload | The paramagnetic properties of iron cause spin dephasing and signal loss, which can be a source of MRE failure, particularly with GRE sequences or imaging at 3 T; however, technical failure is mostly seen in cases with moderate to severe iron overload and can be overcome with the use of SE-EPI sequences | Patients with suspected or diagnosed liver iron overload should be scanned using SE-EPI sequences; 1.5-T magnets are preferred over 3-T magnets |
| Improper interpretation | For maximal diagnostic performance, MRE interpretation should follow quality standards; for example, measurements taken too close to the liver capsule can be unreliable; patient motion can degrade MRI data and result in unreliable MRE (ie, whole liver crossed out by the confidence map) | Compliance with standardized interpretation guidelines and recognition of common pitfalls and limitations are key for proper interpretation; readers are referred to the QIBA MRE profile (10) and to the Interpretation and Reporting section and Appendix S1 of this article |

Note.—GRE = gradient-recalled-echo imaging, MRE = MR elastography, QIBA = Quantitative Imaging Biomarkers Alliance, SE-EPI = spin-echo echo-planar imaging.

1-year progression risk when liver stiffness is less than 3.3 kPa (29). For patients with MAFLD, MRE may help differentiate those at risk for progressing to advanced stages from those with simple steatosis (30). In a prospective MAFLD study, a 15% increase in elastography-derived liver stiffness was associated with histologic progression to advanced fibrosis or cirrhosis (31).

Decompensation and death were more common in patients with MAFLD-related advanced fibrosis or cirrhosis who had serially increasing liver stiffness compared with those who had unchanged stiffness (30,32). MRE has also shown promise in stratifying the risk of variceal bleeding and the development of hepatocellular carcinoma in patients with advanced liver disease (33,34). In a study of patients with sustained hepatitis C virologic response, the risk of hepatocellular carcinoma development at 1, 2, and 3 years was 6.6%, 11.9%, and 14.5%, respectively, for patients with liver stiffness of 3.75 kPa or greater,

**Table 2: Diagnostic Performance of MR Elastography for Staging Liver Fibrosis Reported in the Literature**

| Population, Study, and Year | Sequence | Field Strength (T) | Fibrosis Stage Thresholds (kPa)* | Sensitivity (%) | Specificity (%) | AUC |
|---|---|---|---|---|---|---|
| Chronic liver disease and healthy volunteers | | | | | | |
| Yin et al, 2007 (59) | 2D GRE | 1.5 | F1: 2.93 | F1: 98 | F1: 99 | F1: 1.0 |
| Choi et al, 2013 (60) | 2D GRE | 1.5 | F1: 2.90 | F1: 91 | F1: 87 | NA |
| Ichikawa et al, 2015 (15) | 2D GRE | 3 | F1: 2.60; F2: 2.80; F3: 3.60; F4: 4.00 | F1: 95; F2: 100; F3: 93; F4: 100 | F1: 100; F2: 97; F3: 99; F4: 98 | F1: 0.99; F2: 1.0; F3: 1.0; F4: 1.0 |
| Various liver diseases | | | | | | |
| Asbach et al, 2010 (61) | SE-EPI | 1.5 | F1: 2.61; F2: 3.00; F3: 3.86; F4: 5.86 | F1: 75; F2: 77; F3: 97; F4: 100 | F1: 94; F2: 97; F3: 87; F4: 90 | F1: 0.92; F2: 0.94; F3: 0.98; F4: 0.99 |
| Wang et al, 2011 (62) | 2D GRE | 1.5 | F2: 5.68; F3: 6.79; F4: 8.06 | F2: 91; F3: 92; F4: 95 | F2: 97; F3: 95; F4: 87 | F2: 0.98; F3: 0.99; F4: 0.95 |
| Singh et al, 2015 (8) | 2D GRE | 1.5 | F1: 3.45; F2: 3.66; F3: 4.11; F4: 4.71 | F1: 73; F2: 79; F3: 85; F4: 81 | F1: 79; F2: 81; F3: 85; F4: 81 | F1: 0.84; F2: 0.88; F3: 0.93; F4: 0.92 |
| Chang et al, 2016 (16) | 2D GRE | 1.5 | F1: 2.90; F2: 2.90; F3: 3.47; F4: 4.65 | F1: 75; F2: 97; F3: 96; F4: 100 | F1: 100; F2: 84; F3: 97; F4: 93 | F1: 0.91; F2: 0.96; F3: 0.99; F4: 0.97 |
| Yoshimitsu et al, 2016 (42) | 2D SE-EPI | 3 | F1: 3.13; F2: 3.85; F3: 4.28; F4: 5.38 | F1: 89; F2: 90; F3: 97; F4: 94 | F1: 92; F2: 90; F3: 92; F4: 82 | F1: 0.89; F2: 0.90; F3: 0.94; F4: 0.85 |
| Cheng et al, 2019 (43) | 2D GRE | 1.5 | F3: 3.70 | F3: 79 | F3: 84 | F3: 0.86 |
| Lefebvre et al, 2019 (27) | 2D GRE | 3 | F1: 2.46; F2: 2.65; F3: 3.32; F4: 4.40 | F1: 89; F2: 90; F3: 88; F4: 89 | F1: 43; F2: 48; F3: 70; F4: 63 | F1: 0.88; F2: 0.85; F3: 0.88; F4: 0.88 |
| Fu et al, 2020 (63) | 2D GRE | 1.5 | F1: 3.16; F2: 3.57; F3: 4.41; F4: 5.10 | F1: 87; F2: 89; F3: 88; F4: 100 | F1: 96; F2: 98; F3: 92; F4: 90 | F1: 0.96; F2: 0.96; F3: 0.96; F4: 0.98 |
| Schawkat et al, 2020 (64) | 2D SE-EPI | 3 | F3: 4.09 | NA | NA | F3: 0.92 |
| Sofue et al, 2020 (56)† | 2D GRE at 60 Hz and 80 Hz | 1.5 | F1: 2.94, 3.20; F2: 3.51, 4.16; F3: 4.68, 4.99; F4: 6.62, 8.33 | F1: 84, 88; F2: 85, 85; F3: 93, 93; F4: 100, 100 | F1: 100, 80; F2: 90, 90; F3: 94, 94; F4: 75, 75 | F1: 0.87, 0.87; F2: 0.87, 0.87; F3: 0.93, 0.93; F4: 0.77, 0.77 |
| Li et al, 2021 (65)† | 2D and 3D SE-EPI | 3 | F1: 2.99, 2.54; F2: 3.25, 2.65; F3: 3.64, 3.15; F4: 3.67, 3.64 | F1: 73, 75; F2: 77, 82; F3: 85, 83; F4: 95, 79 | F1: 100, 96; F2: 96, 95; F3: 95, 98; F4: 75, 91 | F1: 0.89, 0.89; F2: 0.91, 0.92; F3: 0.94, 0.95; F4: 0.92, 0.93 |
| Sato et al, 2021 (66) | 2D GRE | 1.5 | F1: 2.70; F2: 2.90; F3: 3.30; F4: 4.00 | F1: 74; F2: 77; F3: 81; F4: 78 | F1: 78; F2: 74; F3: 84; F4: 85 | F1: 0.81; F2: 0.84; F3: 0.90; F4: 0.86 |
| Chronic hepatitis B | | | | | | |
| Lee et al, 2014 (67) | 2D GRE | 1.5 | F1: 2.45; F2: 2.69; F3: 3.04; F4: 3.94 | F1: 92; F2: 95; F3: 95; F4: 95 | F1: 98; F2: 96; F3: 94; F4: 95 | F1: 0.99; F2: 0.99; F3: 0.99; F4: 0.99 |
| Venkatesh et al, 2014 (68) | 2D GRE | 1.5 | F1: 2.74; F2: 3.20; F3: 3.70; F4: 4.33 | F1: 96; F2: 97; F3: 100; F4: 100 | F1: 92; F2: 100; F3: 94; F4: 95 | F1: 0.99; F2: 0.99; F3: 0.99; F4: 0.98 |

**Table 2 *(continues)***

**Table 2 (*continued*): Diagnostic Performance of MR Elastography for Staging Liver Fibrosis Reported in the Literature**

| Population, Study, and Year | Sequence | Field Strength (T) | Fibrosis Stage Thresholds (kPa)* | Sensitivity (%) | Specificity (%) | AUC |
|---|---|---|---|---|---|---|
| Chang et al, 2016 (16) | 2D GRE | 1.5 | F1: 2.56; F2: 2.57; F3: 2.92; F4: 3.67 | F1: 85; F2: 91; F3: 89; F4: 84 | F1: 100; F2: 96; F3: 88; F4: 91 | F1: 1.0; F2: 0.90; F3: 0.95; F4: 0.90 |
| Hennedige et al, 2017 (69) | 2D GRE | 1.5 | F2: 3.50; F3: 4.30; F4: 6.50 | F2: 97; F3: 100; F4: 100 | F2: 100; F3: 94; F4: 95 | F2: 0.99; F3: 0.99; F4: 0.98 |
| Cheng et al, 2019 (43) | 2D GRE | 1.5 | F3: 3.63 | F3: 79 | F3: 84 | F3: 0.86 |
| Chronic hepatitis B or C | | | | | | |
| Ichikawa et al, 2012 (70) | 2D GRE | 1.5 | F1: 2.30; F2: 3.20; F3: 4.00; F4: 4.60 | F1: 96; F2: 89; F3: 87; F4: 100 | F1: 100; F2: 100; F3: 100; F4: 86 | F1: 0.98; F2: 0.99; F3: 0.97; F4: 0.98 |
| Shi et al, 2016 (71)† | 2D GRE and 3D SE-EPI | 3 | F1: 3.08, 2.45; F2: 3.13, 2.79; F3: 3.74, 3.28; F4: 4.18, 3.57 | F1: 84, 87; F2: 86, 95; F3: 94, 100; F4: 97, 97 | F1: 98, 96; F2: 85, 91; F3: 91, 91; F4: 89, 90 | F1: 0.95, 0.96; F2: 0.96, 0.97; F3: 0.98, 0.99; F4: 0.98, 0.98 |
| Shi et al, 2021 (17) | 3D SE-EPI | 3 | F1: 2.30; F2: 2.65; F3: 2.86; F4: 3.38 | F1: 77; F2: 90; F3: 100; F4: 100 | F1: 90; F2: 99; F3: 88; F4: 92 | F1: 0.91; F2: 0.97; F3: 0.98; F4: 0.98 |
| MAFLD and MASH | | | | | | |
| Chen et al, 2011 (72) | 2D GRE | 1.5 | F1: 2.74 | F1: 94 | F1: 73 | F1: 0.93 |
| Kim et al, 2013 (73) | 2D GRE | 1.5 | F3: 4.15 | F3: 85 | F3: 93 | F3: 0.95 |
| Loomba et al, 2014 (74) | 2D GRE | 3 | F1: 3.02; F2: 3.58; F3: 3.64; F4: 4.67 | F1: 55; F2: 66; F3: 86; F4: 80 | F1: 91; F2: 92; F3: 91; F4: 94 | F1: 0.84; F2: 0.86; F3: 0.92; F4: 0.89 |
| Imajo et al, 2016 (75) | 2D GRE | 3 | F1: 2.50; F2: 3.40; F3: 4.80; F4: 6.70 | F1: 75; F2: 87; F3: 75; F4: 91 | F1: 86; F2: 85; F3: 87; F4: 95 | F1: 0.80; F2: 0.89; F3: 0.89; F4: 0.97 |
| Loomba et al, 2016 (76)† | 3D SE-EPI | 3 | F3: 3.80, 3.40, 2.43 | F3: 87, 87, 100 | F3: 94, 86, 94 | F3: 0.92, 0.93, 0.98 |
| Singh et al, 2016 (77) | Multiple‡ | 1.5 | F1: 2.88; F2: 3.54; F3: 3.77; F4: 4.09 | F1: 75; F2: 79; F3: 83; F4: 88 | F1: 77; F2: 81; F3: 86; F4: 87 | F1: 0.86; F2: 0.87; F3: 0.90; F4: 0.91 |
| Park et al, 2017 (78) | 2D GRE | 3 | F1: 2.65; F2: 2.86; F3: 2.99; F4: 3.35 | F1: 77; F2: 79; F3: 78; F4: 75 | F1: 79; F2: 82; F3: 80; F4: 81 | F1: 0.82; F2: 0.89; F3: 0.87; F4: 0.87 |
| Furlan et al, 2020 (79) | 2D GRE | 1.5 | F2: 3.0, 2.6, 3.4; F3: 3.4, 3.2, 3.4 | F2: 69, 90, 52; F3: 87, 91, 87 | F2: 88, 53, 94; F3: 97, 89, 92 | F2: 0.85; F3: 0.95 |
| Han et al, 2020 (32) | 2D GRE | 3 | F4: 3.99 | F4: 97 | F4: 93 | F4: 0.95 |
| Imajo et al, 2020 (18) | 2D SE-EPI | 3 | F1: 2.92; F2: 3.19; F3: 3.90; F4: 4.62 | F1: 78; F2: 90; F3: 83; F4: 95 | F1: 100; F2: 81; F3: 92; F4: 75 | F1: 0.95; F2: 0.93; F3: 0.94; F4: 0.92 |
| Tang et al, 2022 (19)† | 2D GRE | 3 | F1: 2.99, 2.98, 3.29; F2: 3.60, 3.65, 3.65 | F1: 68, 66, 50; F2: 93, 93, 93 | F1: 94, 96, 96; F2: 95, 95, 93 | F1: 0.81, 0.95, 0.74; F2: 0.95, 0.95, 0.93 |
| Zhang et al, 2022 (24) | 2D GRE | 3 | F1: 2.60; F2: 3.06; F3: 3.17; F4: 3.42 | F1: 58; F2: 81; F3: 81; F4: 67 | F1: 91; F2: 91; F3: 91; F4: 90 | F1: 0.81; F2: 0.94; F3: 0.95; F4: 0.92 |
| Alpha-1 antitrypsin deficiency | | | | | | |

**Table 2 (*continues*)**

**Table 2 (*continued*): Diagnostic Performance of MR Elastography for Staging Liver Fibrosis Reported in the Literature**

| Population, Study, and Year | Sequence | Field Strength (T) | Fibrosis Stage Thresholds (kPa)* | Sensitivity (%) | Specificity (%) | AUC |
|---|---|---|---|---|---|---|
| Kim et al, 2016 (80) | 2D GRE | 3 | F1: 3.0 | F1: 80 | F1: 100 | F1: 0.89 |
| Autoimmune hepatitis | | | | | | |
| Wang et al, 2017 (81) | 2D GRE | NA | F3: 4.10; F4: 4.50 | F3: 90; F4: 92 | F3: 100; F4: 96 | F3: 0.97; F4: 0.98 |
| Severe to morbid obesity | | | | | | |
| Chen et al, 2017 (82) | 2D GRE | 1.5 | F1: 2.60; F2: 3.50; F3: 3.60; F4: 4.52 | F1: 81; F2: 82; F3: 84; F4: 82 | F1: 63; F2: 90; F3: 83; F4: 91 | F1: 0.83; F2: 0.93; F3: 0.92; F4: 0.95 |
| Pediatrics (<21 y old) | | | | | | |
| Trout et al, 2018 (83) | 2D GRE | 1.5 | F1: 2.41; F3: 4.55 | F1: 69; F3: 86 | F1: 74; F3: 78 | F1: 0.70; F3: 0.90 |
| Pediatric MAFLD | | | | | | |
| Schwimmer et al, 2017 (84)† | 2D GRE | 3 | F1: 2.77, 2.69; F3: 3.05, 3.03 | F1: 44, 47; F3: 50, 33 | F1: 91, 89; F3: 92, 94 | F1: 0.72, 0.72; F3: 0.89, 0.90 |

Note.—AUC = area under the receiver operating characteristic curve, GRE = gradient-recalled-echo imaging, MAFLD = metabolic dysfunction–associated fatty liver disease, MASH = metabolic dysfunction–associated steatohepatitis, NA = not available, SE-EPI = spin-echo echo-planar imaging, 3D = three-dimensional, 2D = two-dimensional.

* Values are the thresholds for discriminating stage F1 or higher, F2 or higher, F3 or higher, and F4.

† For studies that reported results for different sequences, frequencies, readers, or stiffness thresholds investigated, the results are separated by commas.

‡ Meta-analysis includes studies with different sequences.

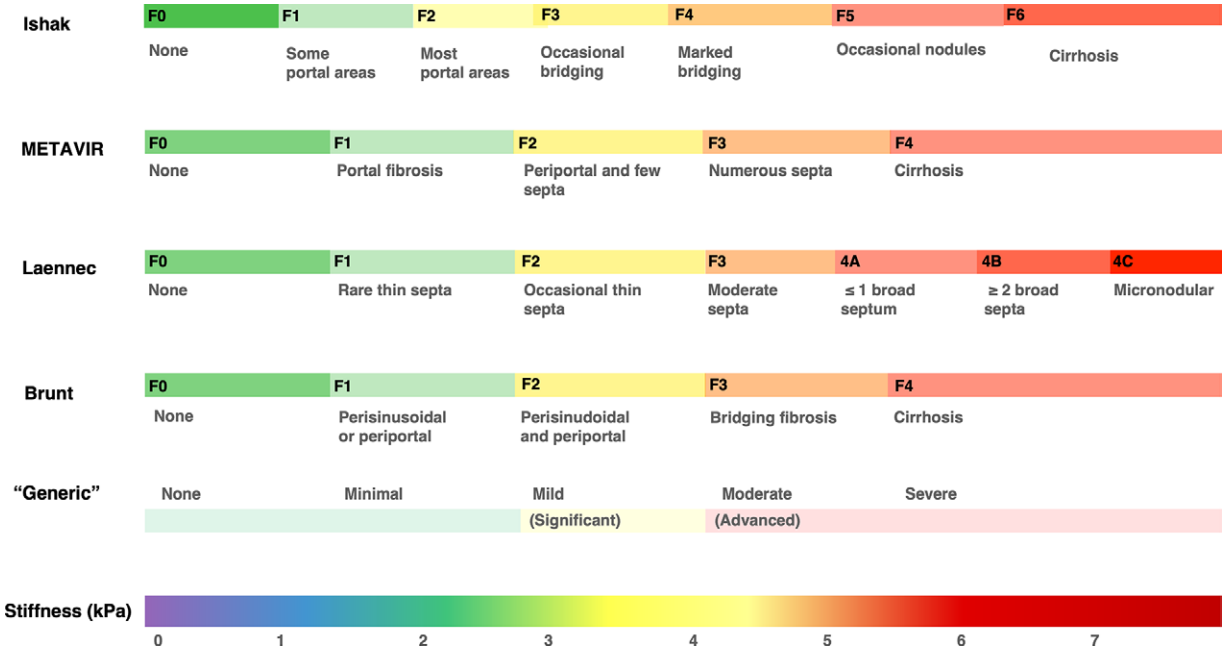


**Figure 4:** Graph shows multiple scoring systems that have been proposed for staging liver fibrosis. These systems differ in their purpose, definitions of fibrosis stages, and subgroups. The use of liver stiffness as a continuous variable has advantages over ordinal categories. It may provide better clinical and prognostic correlation, especially given that most staging systems group patients with cirrhosis in a single category, without taking into consideration the severity of cirrhosis or any longitudinal histologic progression or regression. Brunt = Brunt scoring system, F = fibrosis stage, Ishak = Ishak score, Laennec = Laennec staging system, METAVIR = Meta-analysis of Histological Data in Viral Hepatitis scoring system.

and diagnostic accuracy was higher for MRE than for serum fibrosis markers (35). Preliminary data suggest that MRE-derived liver stiffness can help predict recurrence risk in patients treated for hepatocellular carcinoma (36).

## Future Directions

### Integrating MRE and Other Noninvasive Biomarkers

To further improve the performance of noninvasive methods, researchers have investigated algorithmic combinations of MRE-derived stiffness and other noninvasive biomarkers (37). Tests can be performed in a sequential or combined approach.

***Sequential approach.***—In the sequential approach, one test, often a blood test or a point-of-care test such as FibroScan (Echosens), is performed first. Depending on the results of the initial test, fibrosis may be ruled out, or further assessment, such as MRE, may be performed. This approach essentially functions as a decision tree.

A prototype of this is MEFIB (MRE plus Fibrosis-4 [FIB-4]) (31), designed to rule in or rule out significant fibrosis. FIB-4 is calculated using the following formula: (age [years] × AST [U/L])/(platelets [$10^9$/L] × ALT [U/L])$^{1/2}$, where AST is aspartate aminotransferase (a serum marker of active liver injury) and ALT is alanine aminotransferase. In this approach, FIB-4 is calculated first. If FIB-4 is less than 1.6, fibrosis is ruled out. If FIB-4 is 1.6 or greater, the patient undergoes MRE, where the threshold for fibrosis is a liver stiffness of 3.3 kPa or greater (indicating ≥F2). The combination of FIB-4 value of 1.6 or greater and MRE-derived liver stiffness of 3.3 kPa or greater has higher diagnostic performance than either method alone or other tests, with a positive predictive value of 97.1% to rule in stage F2 or greater, potentially identifying patients eligible for treatment without invasive biopsy (Fig 5) (26,38).

Preliminary studies also indicate that MEFIB has excellent negative predictive value for clinical outcomes such as gastrointestinal varices requiring treatment, ascites, and hepatic encephalopathy (39,40). Until now, the application of MEFIB has been simulated using data from research studies in which all participants underwent FIB-4 calculation and MRE, but the prospective performance MEFIB as a decision tree has not been investigated. Other sequential approaches have been proposed, including combining vibration-controlled transient elastography–derived stiffness, controlled attenuation parameter, and AST (41), However these approaches show lower diagnostic performance and have not been systematically investigated. Theoretical advantages of sequential approaches are that they mirror current clinical practice, can be integrated into clinical care pathways, and are cost-effective in that they reduce the number of unnecessary tests.

***Combined approach.***—In the combined approach, two or more tests are performed simultaneously, with the values from each test integrated into a single equation, rather than following a decision tree. A prototype of this approach is MRI-AST (MAST), designed to rule in or rule out progressed forms of MAFLD defined by high inflammatory activity, that is, metabolic dysfunction–associated steatohepatitis (MASH) activity score of 4 or greater and fibrosis stage of F2 or greater (called fibro-MASH). Individuals with fibro-MASH are potential candidates for pharmacologic treatment, but their identification in clinical practice may be challenging due to the lack of specific symptoms. AST serves as a marker of active liver injury, and an MRI- and serum-based score could potentially help identify these patients. To compute MAST, AST, MRI proton density fat fraction (PDFF), and MRE-derived stiffness are assessed. The values of the three tests are combined using the following formula: MAST = expit(−12.17 + 7.07 log[stiffness] + 0.037 × PDFF + 3.55 log[AST]), where expit($x$) = exp($x$)/(1 + exp[$x$]). MAST scores of less than 0.165 and 0.242 or greater are used for ruling out and ruling in fibro-MASH, respectively (Fig 6) (42).

Sensitivity and negative predictive value for the rule-out cutoff and specificity and positive predictive value for the rule-in cutoff are 90% or greater (43). The few patients with MAST scores between these two values are considered in the "gray zone," and further work-up may be required, including potential liver biopsy for definitive diagnosis. Preliminary data indicate that MAST score has higher diagnostic performance and a lower rate of indeterminate results than other noninvasive biomarkers for identifying patients with fibro-MASH (38,44). Other combined approaches have also been proposed. The combination of MRE-derived liver stiffness, MRI proton density fat fraction, and serum markers has shown high discriminatory performance in differentiating

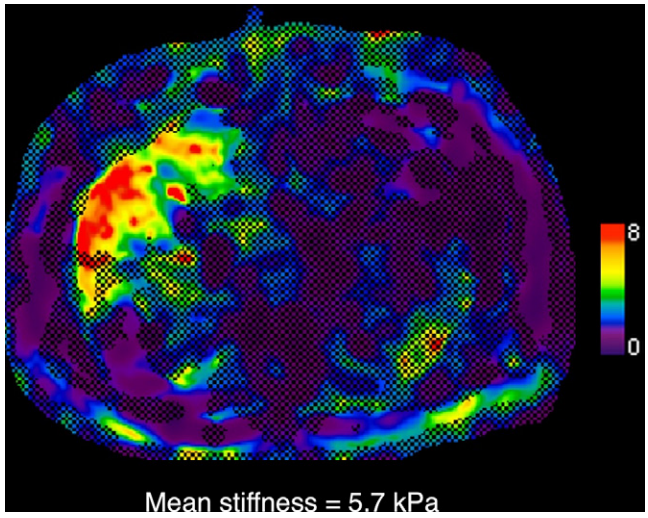


**Figure 5:** Example of the MR elastography (MRE) plus Fibrosis-4 (FIB-4) (MEFIB) sequential approach used to rule in or rule out significant fibrosis in a 66-year-old man with clinical suspicion of significant fibrosis. A FIB-4 value of 5.15 (higher than the ≥1.6 threshold) computed from age, aspartate aminotransferase, alanine transaminase, and platelet count justified proceeding to MRE, which revealed a mean stiffness of 5.7 kPa. The axial elastogram represents a stiffness map expressed in kilopascals, on a scale from 0 to 8 kPa, where low stiffness is represented in purple and high stiffness in red, with a confidence mask overlaid (hatching). The combination of a FIB-4 value of 1.6 or greater and an MRE-derived liver stiffness of 3.3 kPa or greater has a high positive predictive value to rule in significant fibrosis (≥F2). A liver biopsy performed in a research setting confirmed cirrhosis (F4) related to metabolic dysfunction–associated steatohepatitis.

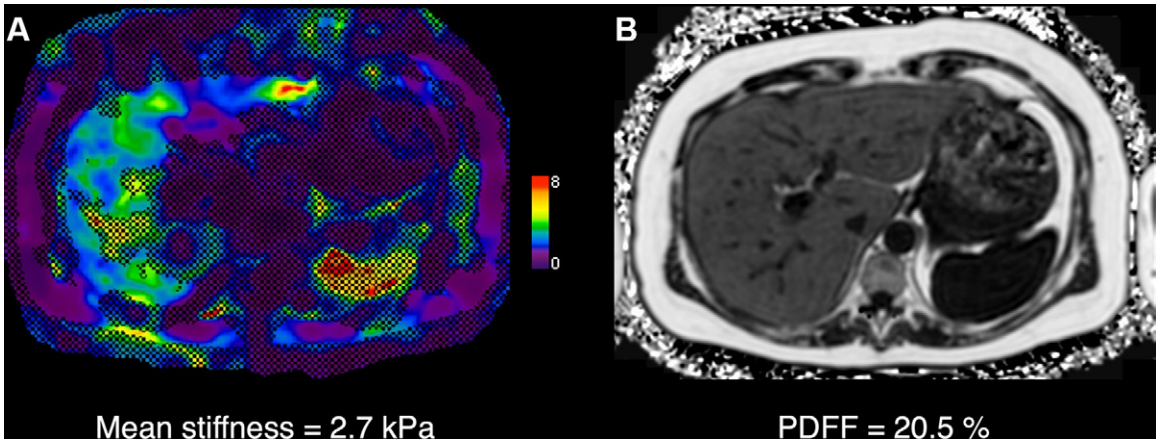


**Figure 6:** Example of the MRI–aspartate aminotransferase (AST) (MAST) combined approach used to rule in or rule out metabolic dysfunction–associated steatohepatitis (MASH) in a 52-year-old woman with clinical suspicion of MASH. The MAST score is computed from MR elastography (MRE)–derived stiffness, MRI proton density fat fraction (PDFF), and AST. **(A)** The axial elastogram represents a stiffness map expressed in kilopascals, on a scale from 0 to 8 kPa, where low stiffness is represented in purple and high stiffness in red, with a confidence mask overlaid (hatching). The mean MRE stiffness was 2.7 kPa. **(B)** MRI proton density fat fraction, determined from the axial MRI scan, was 20.5%, indicating moderate to severe steatosis. With an AST value of 144 U/L, the computed MAST score was 0.332. A value of 0.242 or higher is used to rule in fibro-MASH (MASH activity score of 4 or greater and fibrosis stage of F2 or greater). A liver biopsy performed in a research setting confirmed a MASH activity score of 5 and a fibrosis stage of F2.

MASH from simple steatosis (45), as has the combination of MRE stiffness with MR relaxation values such as T1, although the latter technique is still limited by technical variability and the lack of a reference standard (45,46). A theoretical advantage of the combined approach is that it uses more data and therefore might have higher diagnostic performance than the sequential approach.

## Other Diagnostic Pathways

Considering the current armamentarium for noninvasive diagnosis and staging of liver fibrosis, well-defined guidelines are needed to determine which test should be performed. These guidelines should consider patient characteristics, available treatment options, and diagnostic performance. This approach aims to more objectively make the decision of which patients should be evaluated with MRE. For example, one potential approach is to initially evaluate patients with serologic tests or point-of-care elastographic techniques, reserving MRE for technically difficult cases (eg, obese patients) or for patients whose initial results were inconclusive.

The high diagnostic performance of MRE, either alone or in combination with other tests, might render liver biopsy unnecessary. This paradigm shift would allow the management of patients with chronic liver disease to rely on MRE or other noninvasive tests, eliminating the need to translate MRE-derived stiffness values to histologic stages. Instead, stiffness values, individually or in combination, could guide management (21). Moreover, MRE-derived liver stiffness as a continuous variable could inform patient selection and surveillance frequency in hepatocellular carcinoma screening programs. It could also impact the pretest probability of malignancy or hepatocellular carcinoma in imaging-based systems like the Liver Imaging Reporting and Data System (LI-RADS) or indicate a need to adjust the LI-RADS category (eg, some LR-3 findings could be upgraded to LR-4 based on liver stiffness criteria).

## Emerging Technologies

Developments on the technical front aim to improve workflow, patient experience, efficiency, image quality, or classification accuracy. Artificial intelligence–based guidance for technologists performing MRE is an unmet need and focus of research. Automated analysis methods can potentially reduce the variability found in manual analysis (47). Free-breathing MRE acquisitions either gated or combined with radial acquisitions improve patient comfort and can improve image quality and performance in critically ill patients and in children (48,49). Flexible passive drivers with better fit on the abdominal wall improve patient comfort (50). The combination of multiple flexible drivers allows coverage of a larger area of the abdomen and stiffness measurements of multiple organs (51).

Multifrequency and three-dimensional (3D) MRE acquisitions have the potential to improve image quality, reproducibility, and disease characterization (34,52). Different 3D MRE–derived parameters for the detection and grading of liver inflammation and its differentiation from early fibrosis have shown promising results. Shi et al (17) distinguished inflammation from early fibrosis using a 3D MRE–derived marker of viscosity in patients with hepatitis B and C virus infections. Khalfallah et al (53) found significant associations between viscoelasticity measured with 3D MRE and histologic features that differentiate MAFLD from MASH. In another study, the combination of 3D MRE parameters (shear stiffness and damping ratio) and proton density fat fraction showed higher performance for diagnosing fibro-MASH than the combination of two-dimensional MRE–derived stiffness and proton density fat fraction (area under the receiver operating characteristic curve = 0.973 vs 0.906, $P = .081$; net reclassification improvement = 0.28, $P < .05$) (54). The improved characterization of these additional parameters using 3D MRE techniques may also help differentiate other coexistent processes in liver disease such as congestion from fibrosis in patients with congenital heart disease (55,56).

### The Need for Improved Access and Community Validation

Although evidence supports the high diagnostic performance of MRE for liver fibrosis assessment, and the technique has had Food and Drug Administration approval since 2009, several barriers to wider adoption remain. MRE is still mostly performed in academic or tertiary centers, with analysis being performed by expert radiologists, which limits patient access. While community practices are starting to adopt the technology, the validation of MRE results in a community setting requires systematic evaluation. Cost may be a potential barrier to adoption; however, recent data show that MRE can be more cost-effective than US-based vibration-controlled transient elastography in patients with MAFLD (57). Further, a quantitative MRI examination limited to MRE as a standalone test costs less and requires less scanning time than a full abdominal MRI examination. While some abbreviated protocols have been proposed (58), studies to validate the performance of these protocols are still needed.

## Conclusion

Considering the current burden of chronic liver disease worldwide, MR elastography (MRE), with very high diagnostic performance in noninvasive staging of liver fibrosis, can better inform treatment options to improve patient care. MRE-derived liver stiffness measurements provide better clinical and prognostic correlation than histologic stages. If needed, guidance from the Society of Abdominal Radiology and the Liver Imaging Reporting and Data System provides simple thresholds for interpretation of MRE-derived stiffness values. Emerging diagnostic techniques that integrate MRE and laboratory tests improve the detection of fibrosis, enhance the classification of disease, and help predict disease progression and treatment response.

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